Zacks Small-Cap Research

Sponsored – Impartial – Comprehensive

July 11, 2018

John D. Vandermosten, CFA
312-265-9588 / jvandermosten@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Suite 1600, Chicago, IL 60606

Heat Biologics Inc (HTBX - NASDAQ)

Heat Biologics: Making an ImPACT on Cancer

Based on our DCF model and a 15% discount rate, Heat Biologics is valued at approximately $5.00 per share. Our model applies a 15% probability of ultimate approval and commercialization for HS-110 in a broad NSCLC setting. The model includes contributions from the US, EU and rest of world.

Current Price (7/10/2018)	$2.23
Valuation	**$5.00**

INITIATION

Heat Biologics has developed two novel immunotherapies designated ImPACT & ComPACT. They utilize genetically-modified cells to secrete a broad array of cancer antigens accompanied by a gp96 adjuvant to stimulate a CD8+ T-cell mediated anti-cancer immune response.

The company's key indication in NSCLC is addressed with portfolio candidates HS-110 and HS-130, both administered in conjunction with checkpoint inhibitors. Heat is currently conducting Phase II trials for HS-110 and expects to begin the HS-130 trial in 4Q:18. Other pipeline constituents emerged from the company's acquisition of Pelican Therapeutics in 2017. Pelican is developing a T-cell co-stimulating antibody targeting the cell surface receptor TNFRSF25 called PTX-35.

The valuation assumes a 2023 FDA approval of HS-110 and a 2023 launch of the compound in the US, followed by a 2024 launch in the EU and global availability by 2025 that will be achieved through the efforts of partners.

SUMMARY DATA

52-Week High	**7.90**
52-Week Low	**1.09**
One-Year Return (%)	**-60.2**
Beta	**1.00**
Average Daily Volume (sh)	**2,167,241**
Shares Outstanding (mil)	**20.8**
Market Capitalization ($mil)	**46.3**
Short Interest Ratio (days)	**0.26**
Institutional Ownership (%)	**1.88**
Insider Ownership (%)	**0.97**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2017 Estimate	**N/A**
P/E using 2018 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	$0.0 A	$0.4 A	$0.5 A	$0.6 A	$1.5 A
2018	$0.8 A	$1.2 E	$1.2 E	$1.2 E	$4.4 E
2019					$4.8 E
2020					$2.8 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2017	-$1.18 A	-$0.91 A	-$0.64 A	-$0.81 A	-$3.08 A
2018	-$0.75 A	-$0.18 E	-$0.14 E	-$0.14 E	-$0.79 E
2019					-$0.76 E
2020					-$0.74 E

*2018 quarterly EPS does not sum due to 2Q share issuance.

© Copyright 2018, Zacks Investment Research. All Rights Reserved.

INITIATING COVERAGE

We are initiating coverage of Heat Biologics Inc (NASDAQ: HTBX) with a $5.00 price target based on our estimates for a 2023 launch of lead compound HS-110. The clinical-stage company is focused on activating T-cells with its off-the shelf ImPACT technology which activates CD8+ T-cells to induce immune responses. Its proprietary approach transforms live, allogenic cancer cells into osmotic pumps that secrete gp96 and tumor-associated peptides. The gp96 ferries the peptides to antigen presenting cells which activate the immune system. The cells used in the vaccine are fully allogenic and contain a broad variety of cancer-specific antigens that are able to stimulate T-cells against the cancer, providing an effective immunotherapy.

Heat is currently conducting an adaptive Phase II trial which is examining the use of HS-110 in combination with a checkpoint inhibitor and potentially other therapies in preparation for a Phase III registrational study. It will enroll up to 120 patients and target NSCLC, adenocarcinoma and squamous cell carcinoma with a readout in 2Q:19. The first ComPACT trial with HS-130 is planned to begin enrolling in 4Q:18 following an IND submission. HS-130 will also be addressing NSCLC. The 2017 acquisition of Pelican Therapeutics compliments Heat's existing portfolio and augments adaptive immune responses using TNFRSF25 and other co-stimulators. We note that Pelican's lead candidate, PTX-35, is currently in preclinical studies, and we anticipate an IND filing by 1Q:19.

Heat's technology is differentiated from other cancer immunology approaches in that it employs a pan-antigen strategy to cancer immunology. This is in contrast to the single epitope/protein identifier used in many CAR-T and other immuno-oncology (IO) therapies which may allow for tumor immune escape and subsequent relapse. The lead compound's ability to activate T-cells makes it a desirable partner for checkpoint inhibitors, which have shown higher efficacy in hot tumors.

Heat's portfolio will additionally allow for a three vector approach to immuno-oncology. Their vaccine, HS-110 has the potential to activate T-cells and their co-stimulatory molecule, PTX-35, has the ability to increase the activity against cancer cells. These two agents combined with an approved checkpoint inhibitor can arrest several steps in the cancer-immunity cycle, thereby increasing the success rates of the multiple drug therapy.

On March 31, 2018, Heat held approximately $9 million in cash on its balance sheet. Modest amounts of capital have been raised over the last several years with public offerings, stock issuances and warrant exercises. The company currently holds no debt. Subsequent to the first quarter's end, Heat closed a net $19 million capital raise. We expect Heat to consume approximately $1 million per month as it continues its Phase II trial work and seeks a partner for subsequent studies. In parallel, majority-owned Pelican will continue its work on PTX-35 with grant money sourced from the CPRIT. The company currently holds sufficient cash to continue operations into 2020.

Based on our timeline, we expect data to be presented from the Phase II NSCLC trial in 2018. Assuming a suitable partner is found, the Phase III should begin before the end of 2019, with results available by late 2020. Given its focus on development, Heat is expected to seek a partner to license and commercialize HS-110 worldwide. Lung cancer is the second most common cancer in men and women, and due to higher smoking rates overseas, is even more prevalent ex-US, providing opportunities for therapy around the globe.

There are multiple legs supporting our favorable thesis for Heat Biologics, including a well-defined mechanism of action which has shown evidence of being complementary to other in-development and existing therapies, preliminary evidence of efficacy for NSCLC and positive safety data for over 200 patients. Additionally, there is a treatment opportunity of ~1.5 million global diagnosed cases per year of NSCLC and low manufacturing costs compared to others in the class. These factors support strong market acceptance for this cancer vaccine which we believe has the potential to differentiate and enhance the performance of a checkpoint inhibitor.

INVESTMENT THESIS

Heat Biologics has identified a biologic therapy designated HS-110 (viagenpumatucel-L) that can stimulate the body's adaptive immunity to eradicate lung cancer cells. The approach employs a vaccine that uses irradiated cancer cells which secrete a specific protein possessing a dual role. This protein, called gp96, can activate anti-cancer specific T cells and also serves as an adjuvant that enhances the immune response. Compelling data from combination work with checkpoint inhibitors may show increased efficacy compared to HS-110 monotherapy. Following anticipated favorable data from the currently active Phase II trial, we anticipate Phase III work will be

conducted with a partner for non-small cell lung carcinoma using the combination of HS-110 and nivolumab. The firm also has two co-stimulators in the pipeline identified as PTX-35 and PTX-15 that were added via the acquisition of Pelican Therapeutics.

HS-110 is an irradiated lung cancer cell line that has been genetically modified using the company's ImPACT technology platform. The modifications allow the cell to secrete a specific heat shock protein (HSP) known as gp96, which transports protein fragments (peptides) into the extracellular space where they engage antigen presenting cells to activate via innate immune mechanisms, thereby stimulating adaptive immunity through major histocompatibility complex (MHC) class I antigen cross presentation.

Current cancer therapies are only modestly effective in NSCLC and many of the more advanced stages of this cancer fail to respond to initial treatment. First-line treatment for NSCLC recently shifted to checkpoint inhibitors; however, most patients still do not respond. Treatment may also include surgery followed by chemo- and radiotherapy, which is also insufficient as the disease progresses. Poor success rates highlight the need for additional approaches. There are a number of other immunotherapy programs in development for NSCLC, including checkpoint inhibitors, angiogenesis inhibitors, EGFR inhibitors, and others. However, they are only effective in a minority of the population treated or tumors develop resistance to the therapy. None of them have provided a dramatic improvement over existing therapies, and it is expected that many years of trial work will be required before uncertain results are generated from competing approaches. In contrast to other immunostimulants which seek a single identifying protein in cancer cells, HS-110 employs a pan-antigen approach which targets multiple uniquely identifiable proteins for cancer cells. Based on our research, we believe the addressable market for HS-110 in NSCLC is over 175,000 patients per year in the United States and a greater number outside the United States due both to a larger population and higher incidence of smoking. HS-110 possesses a favorable safety profile based on the low incidence of adverse effects in the previous Phase I trials suggesting greater patient uptake.

The agent's promising results support pricing the drug in line with other immune-oncology agents. Many of these therapies present an average cost of above $100 thousand per course of treatment in the United States. Our forecasts maintain a conservative view, and anticipate a discount to these levels that is expected to capture market share. We make further reductions for regions ex-US to reflect relative prices in these economic areas.

While our target price is generated based solely on success in NSCLC, there may be additional cancer indications that can be addressed with the ImPACT or ComPACT platforms and other candidates in Heat's portfolio that may eventually generate revenues. Our analysis does not reflect the benefit of participation in an expedited program by the FDA and assumes a Phase III trial will be required before HS-110 is approved.

Key reasons to own Heat Biologic's shares:

- **Compelling preclinical and clinical data supportive of effective mechanism of action**
- **Differentiated approach that employs multiple proteins for cancer cell identification**
- **Evidence of synergy with checkpoint inhibitors**
- **May address critical need for complementary therapies in NSCLC**
- **Pipeline of additional co-stimulatory assets complementary to HS-110**
- **Favorable drug safety profile with minimal adverse events**
- **Biologic eligible for 12 years of exclusivity in United States**
- **Global rights to intellectual property**
- **Manufacturing process produces high yields at low cost, in contrast to other biologics**

In the following sections we describe the mechanism of action for HS-110. We also discuss HS-110's clinical data and the design of the Phase II trial, which we anticipate will be followed by a Phase III trial conducted in conjunction with a partner. We anticipate initial Phase II data to be shared with potential suitors and regulatory agencies over the next year in order to attract capital, gain attention from large pharmaceutical players focused on the cancer space and develop an effective path forward. HS-110 may help revolutionize cancer therapy by providing a vaccine-based agent that stimulates a cancer patients' immune system, bringing to bear the innate and adaptive systems to clear the body of this disease.

Cancer Vaccines

A vaccine is a biological agent that stimulates the body's adaptive immune system to identify a particular disease, destroy it and recognize and eliminate similar threats in the future. Vaccines can be prophylactic similar to the flu shot or they can be therapeutic and attempt to remediate an existing health problem. Cancer vaccines have a similar profile and are used to either prevent a cancer from developing, such as Gardasil for human papillomavirus, or to treat existing cancer, such as Sipuleucel-T for prostate cancer. Vaccines help boost and stimulate the immune system to protect the body against infectious agents and viruses. The body's adaptive immune system is able to recognize the antigens that are present in the infectious agent and remember them in case of future attacks on the body. This ability to recognize on subsequent exposure is the durable benefit provided by the vaccine as it contains the unique identifiers, or antigens, that are present in invading bacteria, viruses or abnormal cells.

HS-110 (viagenpumatucel-L)

HS-110 (viagenpumatucel-L) is a cancer vaccine derived from NSCLC immortalized cell lines that secrete cancer-specific antigens via gp96, awakening the adaptive immune system to recognize cancer cells and attack them. The biological agent is sourced from an immortalized cell line and contains numerous antigens that are also present in NSCLC tumor cells. The agent is also allogenic, and therefore does not require samples from the patient to develop the therapy. This is in contrast to the well-known CAR-T and other immuno-oncology approaches which require the patient's own cells and significant time and cost for personalized processing.

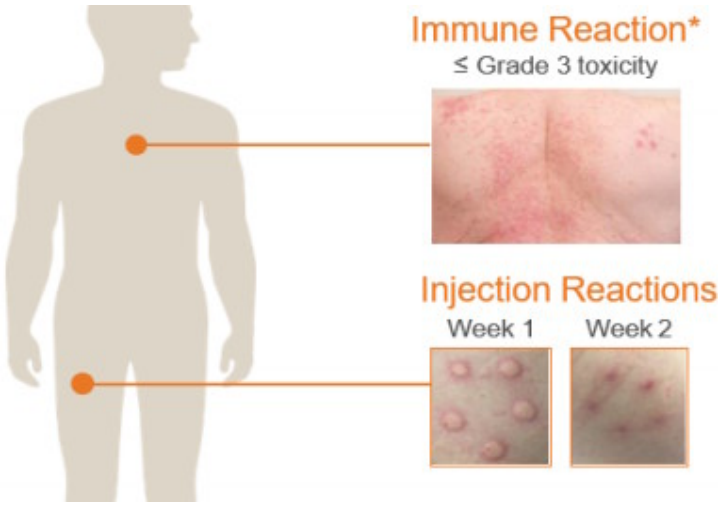
The vaccine cell line that is used in the manufacture of HS-110 is designated AD100. It was taken from an NSCLC patient in 1994 at the University of Miami. The donor was a 74-year old white male who suffered from pelvic pain and bone erosion due to metastatic pulmonary adenocarcinoma.

HS-110 Mechanism of Action

HS-110 has been developed using the company's ImPACT technology which obtains a cancer cell line and modifies the individual cells to act as osmotic pumps secreting antigens uniquely associated with cancerous cells. The ImPACT cells contain a protein called gp96, which is responsible for chaperoning proteins while they fold and resides in the endoplasmic reticulum, retained by the KDEL amino acid sequence. Heat Biologic's process deletes the KDEL leash, which allows gp96 to migrate from the cell, still containing the complement of proteins (antigens) that uniquely identify a tumor and activates the innate and adaptive immune system. The body's innate immune system recognizes gp96, a heat shock protein, and interprets the associated protein as an antigen. These antigens activate the body's CD8+ killer T-cells which then proliferate and seek other cells with similar antigens. The killer T-cells are able to identify the cancerous cells and destroy them. The HS-110 cells are irradiated to prevent them from replicating when injected into the patient.

HS-110 employs allogeneic NSCLC tumor cells as a source of tumor antigens escorted by secreted gp96-Ig and cross-presented via MHC I to patient CD8+ T-cells. This approach assumes that the diversity of tumor antigens that exists in the NSCLC vaccine cell line will match the array of antigens in the patient's tumor. HS-110 is administered via an intradermal injection consisting of a series of five shots in the shoulder and chest.

Exhibit I – Intradermal Injection

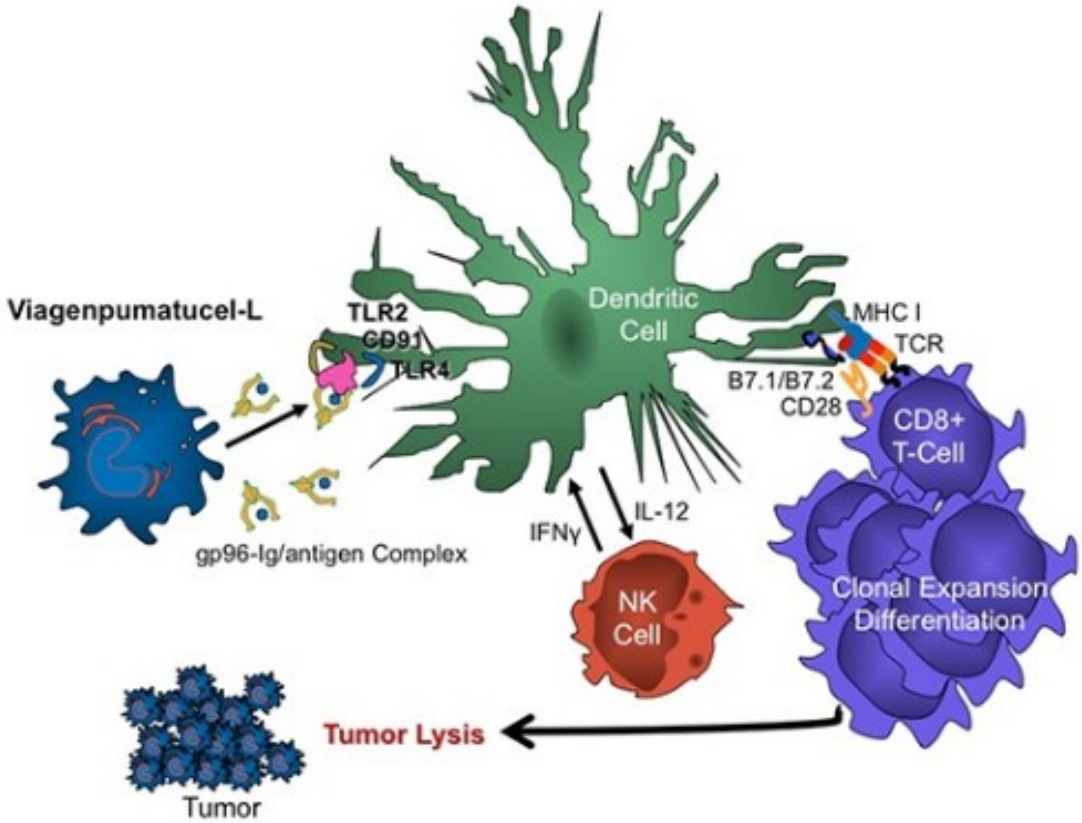


Cancer cells are able to evade the immune system using several methods such as suppressing T-cells, recruiting regulatory T-cells and myeloid-derived suppressor cells, down-regulating MHC receptors or by expressing inhibitory checkpoint molecules such as CTLA-4, PD-L1 and others. This variety of mechanisms helps the cancer thrive. Consequently, a successful immunotherapy must challenge the cancer at multiple parts in the immunity cycle and generate a variety of tumor associated antigens necessary to overcome these defenses.

Below we provide detail regarding HS-110's mechanism of action:

1) NSCLC immortalized cancer cell lines are identified
2) ImPACT technology deletes the KDEL leash which tethers gp96 to the endoplasmic reticulum
3) KDEL is replaced with an IgG domain
4) Cell lines secrete overexpressed cancer associated antigens bound to gp96 which match antigens present in patient's tumor
5) The innate and adaptive arms of the immune system recognize the gp96 antigen complexes secreted by the cancer cell lines
6) Gp96 acts as an adjuvant to activate innate immune signals via TLR2 and TLR4 that mature dendritic cells to express co-stimulatory molecules that activate T-cells when stimulated with antigen
7) Gp96 also serves to activate an adaptive CD8+ T-cell response by cross-presenting (via CD91) antigenic peptides directly to CD8+ T-cells via MHC Class I
8) Consequentially, killer T-cells activate and proliferate seeking matching mutated proteins in tumor cells
9) Pan-antigen cytotoxic T-cell attack launched against cancer cells
10) Upon recognition, the T-cells will destroy live tumor cells
11) Some killer T-cells remain that may keep the body tumor-free when re-challenged with the cancer

Exhibit II – HS-110 (Viagenpumatucel-L) Mechanism of Action



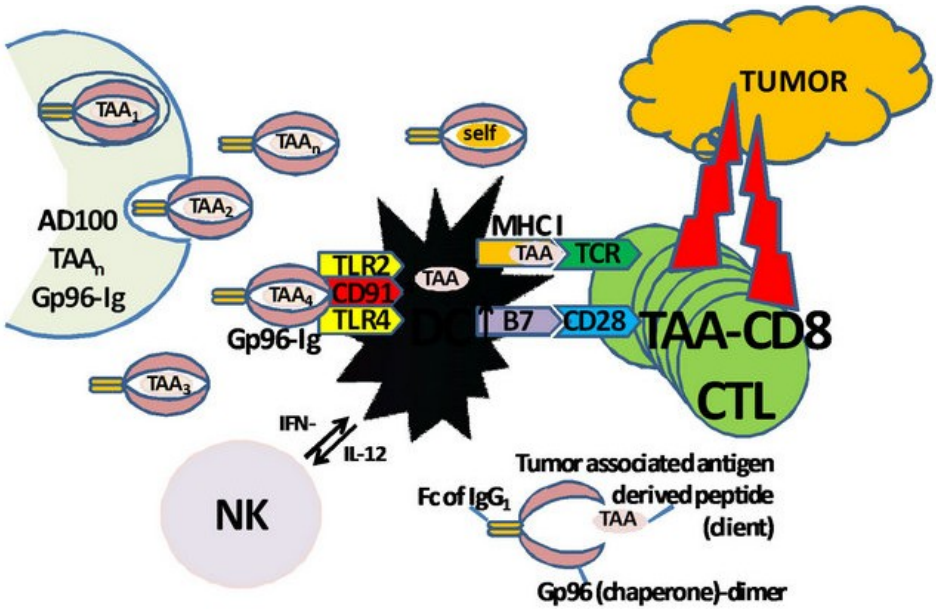
Gp96

Gp96 is a heat shock protein (HSP) responsible for chaperoning proteins, translated by mRNA, as they fold into their final forms. HSPs are produced by cells that are under stress, and may be more accurately described as cellular stress proteins. They were first identified when Italian geneticist, Ferruccio Ritossa, was exposing fruit fly chromosomes to high, but non-lethal temperatures. This led to further research which identified HSPs as molecular chaperones important for proper protein folding and the intracellular movement of proteins. HSPs are expressed in all eukaryotic and prokaryotic species and contribute to the assembly, stabilization, folding and translocation of proteins.

In a healthy cell, gp96 is tethered to the endoplasmic reticulum with a KDEL leash and in this location it comes into contact with almost all proteins and peptides that are present in a cell, including any viruses or intracellular parasites that may be present. Gp96 also may chaperone tumor-associated antigens expressed by tumor cells. When a cell undergoes necrosis, due to infection, trauma or numerous other factors not including apoptosis, the KDEL leash is severed and gp96 and its chaperoned peptides are released into the extracellular environment. The receptor for gp96 is CD91, also known as the scavenger receptor which allows dendritic cells (DCs) to recognize the HSP. After the DC absorbs the proteins, it is dissociated from gp96 and is then cross-presented via MHC I CD8+ T-cells. Gp96 also functions as an adjuvant, stimulating the release of cytokines and chemokines providing a molecular warning signal when necrotic cell death occurs and helping identify released peptides as potential threats thereby generating a powerful immune response.

GP96 and Cancer Immunotherapy

Exhibit III –Representation of gp96 Presenting Antigens[1]



ImPACT

The ImPACT (immune pan-antigen cytotoxic therapy) technology is used to generate gp96 secreting cells from an irradiated immortalized cell line. The technology deletes the tether that attaches gp96 to the cell's endoplasmic reticulum and allows the heat shock protein to transport associated antigens out of the cell. These peptides represent cancer antigens that exist in tumors and are recognized by the patient's immune system. ImPACT engages the body's natural molecular warning system that is specific to CD8+ cytotoxic T-cell immune responses. ImPACT differentiates itself from other immunotherapies in that it is an off-the-shelf approach that does not require any material from the patient. The approach also employs a plurality of unique proteins that identify a specific cancer, reducing the potential for immune escape through mutation. The therapy is specific to CD8+ T-cells and is able to stimulate a response at normal levels of antigen.

[1] http://file.scirp.org/Html/2-2560013/58883597-da93-4e5f-81da-70d6dc157c27.jpg

Exhibit IV – Comparison of ImPACT with Other Immunotherapies[2]

Criteria/Benchmarks	*ImPACT* Therapy	Other Allogeneic	Autologous Cell-based
Pan-antigen delivery (known and unknown)	✓	Some	Some
Targeted delivery of antigens to APC In Vivo	✓	✗	✗
Delivery of antigen selectively via MHC-I molecules	✓	✗	✗
Cross-presentation of antigen to cytotoxic $CD8^+$ T Cells	✓	✗	✗
Exclusive cytotoxic $CD8^+$ T cell response / **No Antibody response**	✓	✗	Some
Synchronous/linked delivery of **antigen-adjuvant**	✓	✗	✗
Antigen specific adjuvant (not general immune stimulants)	✓	✗	✗
Rapid New Product Development	✓	✗	✗

ComPACT (HS-130)

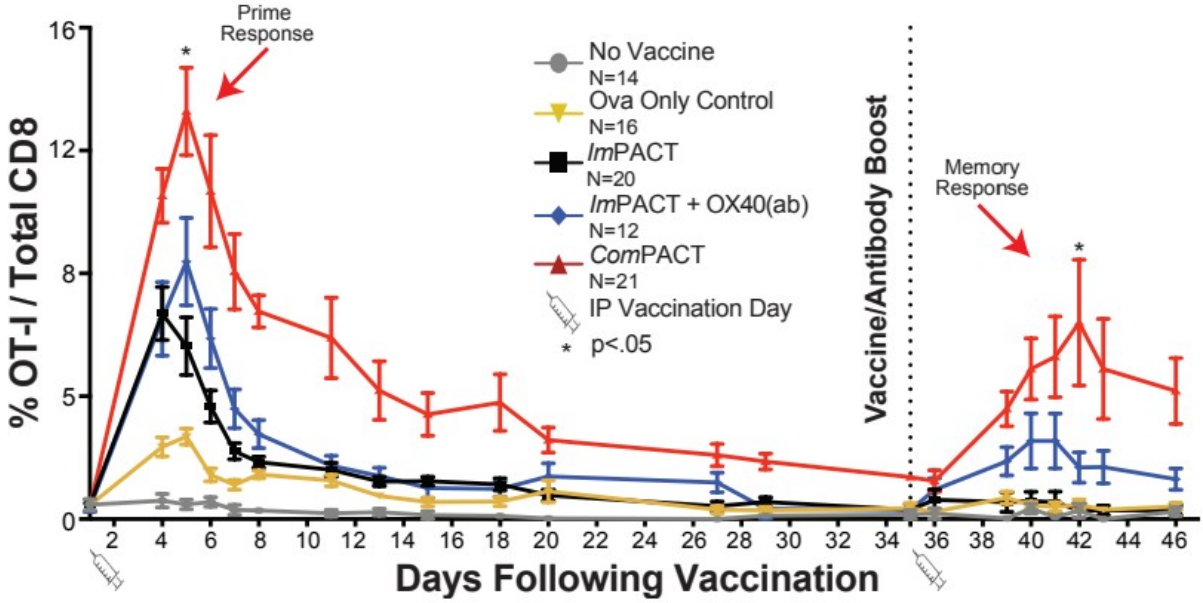
ComPACT (combination pan-antigen cytotoxic therapy), also called HS-130, is a next generation ImPACT therapy that combines gp96 with the T-cell co-stimulator OX40L-Fc, which are both secreted from the same cell. ComPACT can stimulate greater expansion of CD8+ T-cells and enhance the development of CD8+ T cell memory. The therapy is injected intradermally and taken up by the immune system similar to the ImPACT process. When the cancer antigens are presented to the T-cell via the MHC complex, OX40L-Fc binds with the OX40 receptors on the T-cell to further stimulate the response. The T-cells then move to the tumor area and eradicate the cancer cells.

As compared to ImPACT, in preclinical models, ComPACT stimulates higher frequency proliferation of antigen-specific CD8+ T-cells. ComPACT also demonstrates greater antigen specificity while avoiding off-target proliferation and systemic inflammatory cytokine stimulation as compared to OX40 agonist monoclonal antibodies. It is also contained in a simple package that contains both the HSP and the costimulatory agent and can be used with other immunotherapy approaches such as checkpoint inhibitors.[3]

In the following exhibit, the T-cell response by the various candidates in the Heat portfolio are compared against a control and no vaccine in an OT-I mouse model. The experiment examines the agents that stimulate T-cells to clonally expand *in vivo*. The strongest response was from ComPACT, which is HS-110 and OX-40 administered together and locally which shows the synergistic effect of a co-stimulator. ImPACT + OX40 was also compared, which administered OX40 systemically and resulted in a lower response vs. ComPACT. ImPACT alone and control studies were also measured. The preclinical *in vivo* CD8+ responses below provide a hint of the improved efficacy that HS-110 may provide when combined with a co-stimulator.

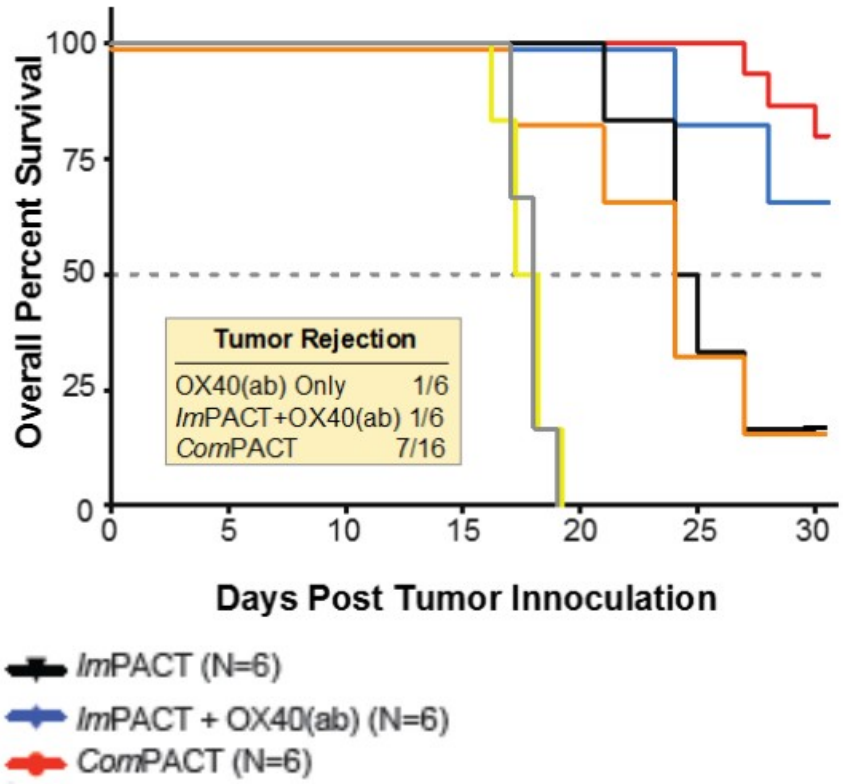
[2] Heat Biologics: http://www.heatbio.com/our-science/impact
[3] Source: Heat Biologics, http://content.stockpr.com/heatbio/files/pages/product-http://content.stockpr.com/heatbio/files/pages/product-pipeline/compact/HTBX_2015_AACR_NYC_ComPACT_Poster.pdf

Exhibit V – Comparison of CD8+ Cell Response ImPACT, ComPACT, et al.



The data from the tumor models show that ComPACT and ImPACT with OX40 stimulate a stronger OT-I / CD8+ response as compared to ComPACT alone. The improved performance is attributed to higher levels of memory precursor cells. In a small size sample, preclinical *in vivo* work has also shown greater survivability with ComPACT as compared to ImPACT or ImPACT+OX40, as shown in the exhibit below.

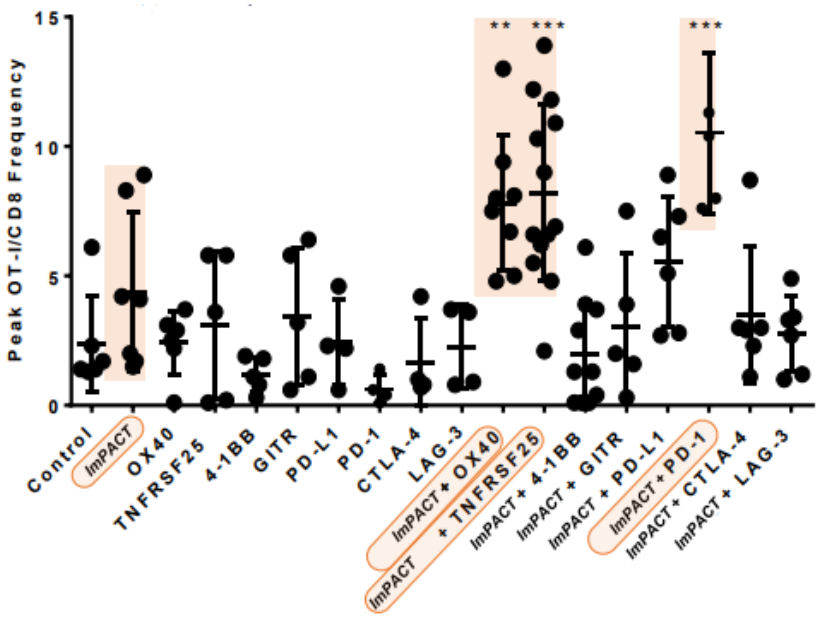
Exhibit VI – Overall Survival for ComPACT, ImPACT & ImPACT+OX40



Heat is now involved with IND-enabling work for ComPACT / HS-130 for the treatment of NSCLC. Manufacturing activities have begun. The current timeline for HS-130 development calls for enrolling the first patient by 4Q:18 and an interim readout by 2Q:19.

Further research adds ImPACT + TNFRSF25 which appears to generate a response on par with ImPACT + OX40. Other combinations are also provided including the addition of several checkpoint inhibitors, PD-1 being the most stimulatory for CD8+ T-cell activation.

Exhibit VII – CD8+ T-cell Activation



PTX-35 and PTX-15

Heat's subsidiary, Pelican, is developing two co-stimulators called PTX-35 and PTX-15. PTX-35 is a humanized, affinity matured monoclonal antibody that acts as an agonist of TNFRSF25, which is a cell surface receptor that mediates apoptotic signaling and differentiation. PTX-15 is a human TL1A-Ig fusion protein, a stabilized form of the natural TNFRSF25 ligand. PTX-35 and PTX-15 both stimulate memory CD8+ cytotoxic T-cells, which eliminate tumor cells and have the potential to expand T-regulatory cells; providing tolerance to allogenic transplantation for bone marrow, heart and islet tissue, replacing maintenance immunosuppression.

Non-small Cell Lung Carcinoma (NSCLC)

According to the American Cancer Society, lung cancer is the second most common cancer in the United States with an estimated 234,000 new cases diagnosed in 2018, which represents about 13% of all cancer diagnoses. While the incidence of lung cancer has fallen over the last two decades due to a decline in smoking habits, it still accounts for one in four cancer deaths, or about 154,000 in 2018. The majority of lung cancer cases are either small cell, which makes up about 13% of the total or non-small cell, which is about 84% of the total. First-line treatment for early-stage NSCLC has historically been surgery followed by chemotherapy and radiation therapy. In more advanced stages, a patient will receive chemotherapy with targeted drugs and in recent years more and more are receiving immunotherapy. Survival for NSCLC in advanced stages is low, with five year survival rates as follows:

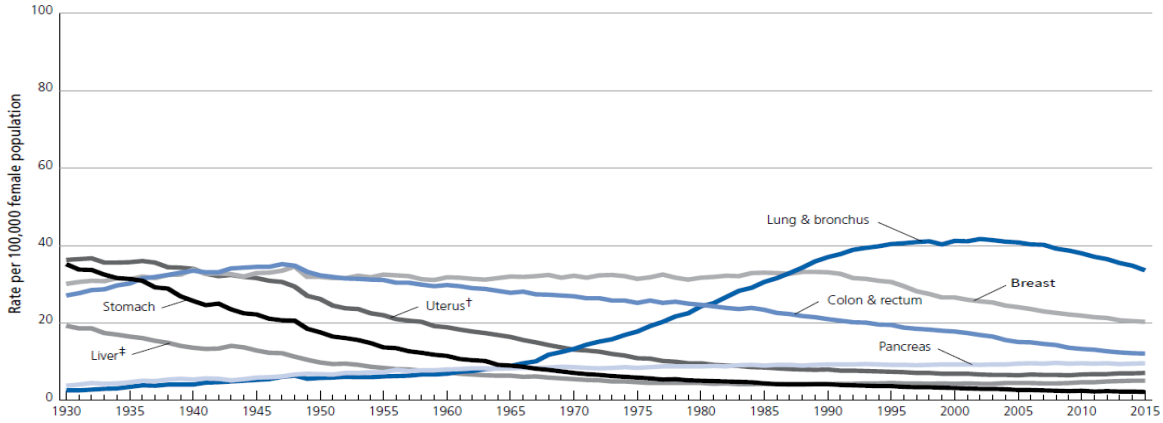
- Stage IA ~49%
- Stage IB ~45%
- Stage IIA ~30%
- Stage IIB ~31%
- Stage IIIA ~14%
- Stage IIIB ~5%.
- Metastatic, or stage IV, ~1%.

NSCLC has several subtypes which include adenocarcinoma, squamous cell (epidermoid) carcinoma, and large cell (undifferentiated) carcinoma which together make up 75% to 85% of cases. Adenocarcinoma is the most common type of NSCLC and is found in the outer areas of the lung. Squamous cell is usually linked to smoking and makes

up 30% of NSCLC. The cancer is located in the lung where the larger bronchi join the trachea to the lung, or in one of the main airway branches. Large cell can be found anywhere in the lung and usually grows and spreads quickly.

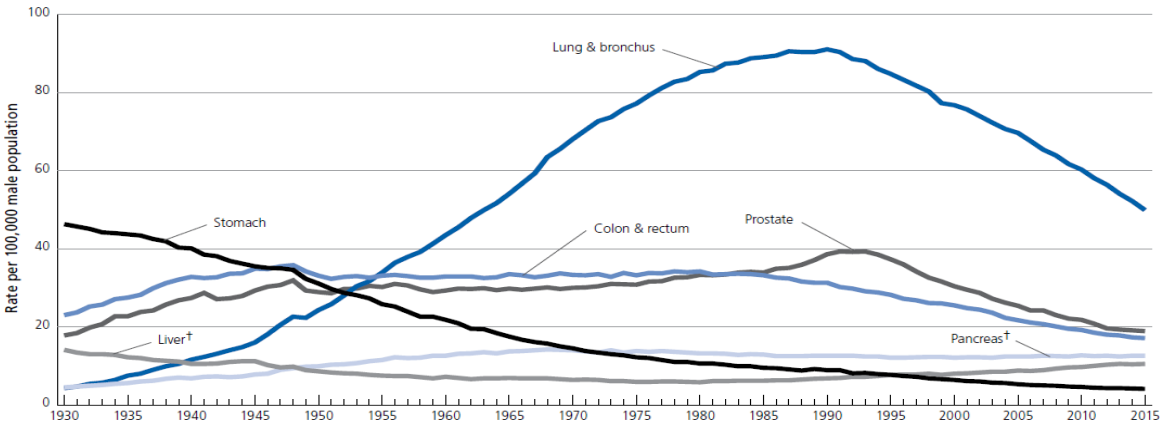
Lung cancer rates are higher in males than in females, likely attributable to higher rates of smoking and exposure to dangerous workplaces substances for men. While lung and bronchus cancer rates are higher in males, the decline in death rate for men has been faster than it has for women over the last 30 years, as shown in the following graphics.

Exhibit VIII - Trends in Age-adjusted Cancer Death Rates* by Site, Females, US, 1930-2015[4]



*Age adjusted to the 2000 US standard population. †Uterus refers to uterine cervix and uterine corpus combined. ‡The mortality rate for liver cancer is increasing.
Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the liver, lung and bronchus, colon and rectum, and uterus are affected by these coding changes.
Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2015, National Center for Health Statistics, Centers for Disease Control and Prevention.
©2018, American Cancer Society, Inc., Surveillance Research

Exhibit IX - Trends in Age-adjusted Cancer Death Rates* by Site, Males, US, 1930-2015[5]



*Age adjusted to the 2000 US standard population. †Mortality rates for pancreatic and liver cancers are increasing.
Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancers of the liver, lung and bronchus, colon and rectum, and uterus are affected by these coding changes.
Source: US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2015, National Center for Health Statistics, Centers for Disease Control and Prevention.
©2018, American Cancer Society, Inc., Surveillance Research

Risk Factors & Symptoms

The most prevalent risk factor for lung cancer is smoking, which is held responsible for 80 to 85% of lung cancers in the US according the American Cancer Society and the Lung Cancer Alliance. Other common risks include exposure to radon, diesel exhaust, asbestos and family history. Carcinogens including industrial chemicals and radioactive agents can also contribute to the incidence of lung cancer. Genetic factors also play a role, especially for the small portion of lung cancers in non-smokers. Symptoms of the disease include a cough that persists, shortness of breath, weight loss and/or coughing up blood.

[4] US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2015, National Center for Health Statistics, Centers for Disease Control and Prevention. ©2018, American Cancer Society, Inc., Surveillance Research.
[5] US Mortality Volumes 1930 to 1959, US Mortality Data 1960 to 2015, National Center for Health Statistics, Centers for Disease Control and Prevention. ©2018, American Cancer Society, Inc., Surveillance Research.

Treatment

Treatment for NSCLC usually includes surgery to remove the tumor and may be preceded or followed by chemotherapy. Used beforehand, chemotherapy may shrink the tumor to make surgery easier. When chemotherapy is used following surgery, it helps prevent the cancer from returning. Radiotherapy is also used to fight the disease. If the cancer returns after these treatments then alternative therapies are considered.

For patients with inoperable disease, platinum-based chemotherapy in conjunction with radiation therapy is recommended. Chemotherapy by itself is recommended for metastatic NSCLC, as the disease is not localized enough for surgery or radiotherapy to work. Response rates for this group range from 15 to 30%, with average survival of less than a year. A meta-analysis of 52 studies found that chemotherapy treatment increased the chance of one-year survival by 10% and median survival by six weeks, making a dramatic case for improved therapies.

Immunotherapy is preferred because it frequently has fewer side effects, maintains its potency, works well in conjunction with other therapies and is also able to better target the disease. Several classes of immunotherapy exist including therapeutic vaccines, checkpoint inhibitors, immune modulators, adoptive cell therapy (CAR-T), oncolytic viruses and antibody drug conjugates among others. One of the most frequently used immunotherapies is the checkpoint inhibitor class, which produces a durable response in approximately 20% of patients with advanced NSCLC. Checkpoints are particularly effective in patients with “hot” tumors, which have immune cells present. To attract and activate immune cells in the tumor, other therapies such as vaccines can be considered to work in conjunction with checkpoints.

Cancer cells have developed methods to escape immune surveillance by downregulating the immune system and converting immune cells into supporters of tumor growth. Furthermore, the variety in tumor composition may allow for progression in certain cancer mutations that are not addressed in treatments with different antigen signatures. This suggests that a polyepitope approach may be more effective as it recognizes several tumor-associated antigens present, reducing the likelihood that rogue tumor cells will escape destruction.

Immunotherapy maintains several key benefits relative to other therapies. By allowing the body to fight the tumor itself, there are generally fewer and less severe side effects. Another serious issue in lung and other cancers, is the cancer’s ability to build immunity to the treatment received. Immunotherapies are less likely to encounter resistance from a cancer as the body’s adaptive immune system can adjust to mutating cancer cells. For Heat’s approach in particular, the presence of numerous cancer-identifying antigens reduces the chance that some tumor cells will elude detection.

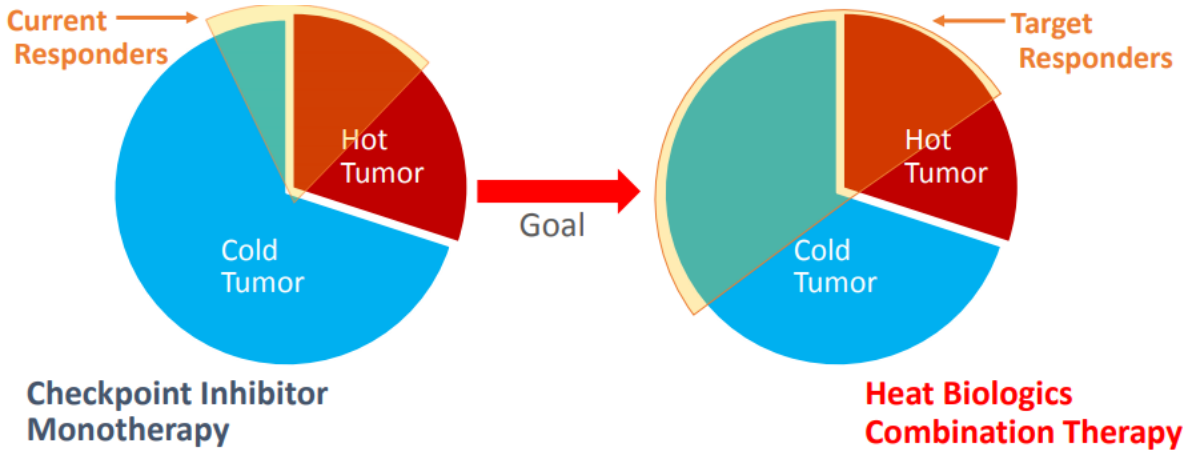
Checkpoint inhibitors such as Merck’s Keytruda (pembrolizumab) and Bristol-Myers’ Opdivo (nivolumab), are approved in several instances of first and second line NSCLC treatment. Checkpoint inhibitors have shown themselves to be very effective in a certain segment of the population, and the search for broader efficacy has prompted efforts using checkpoint inhibitors in combination with other therapies that can potentially provide a synergistic effect. Currently, HS-110 is in a Phase I/II combination trial with nivolumab for non-small cell lung adenocarcinoma in patients who have failed at least one prior line of therapy for incurable or metastatic disease.

Exhibit X – Keytruda and Opdivo



Heat envisions the benefit of combination therapy to improve the response rate for checkpoint inhibitors. The company cites a 17% to 20% response rate[6,7] for monotherapy anti-PD-L1 patients, represented by the red portion of the graph. With the addition of HS-110 or HS-130, target responders could increase the effectiveness of checkpoints by expanding the proportion of cold tumors where the therapy works.

Exhibit XI – Potential for Combination Therapy with Checkpoint Inhibitors



Competing/Complementary Therapies in Development for NSCLC

NSCLC is a therapeutic area with substantial unmet need. Many research pharmaceutical companies have recognized this and are exploring the use of currently approved drugs for as-yet non-approved indications and working on developing new compounds to address the disease. Below we highlight several of the key therapies that are either approved or in development.

Exhibit XII – Competing Products in Development for NSCLC

Generic Name	Brand Name	Class
Avastin	Bevacizumab	Antiangiogenic agents
Cyramza	Ramucirumab	Antiangiogenic agents
Ofev	Nintedanib	Antiangiogenic agents
Alimta	Pemetrexed	Antifolate agent
Nivolumab	Opdivo	Checkpoint Inhibitor
Pembrolizumab	Keytruda	Checkpoint Inhibitor
Imfinzi	Vinorelbine.	Checkpoint Inhibitor
Gemzar	Gemcitabine	Chemotherapy
Paraplatin	Carboplatin	Chemotherapy
Taxol	Paclitaxel	Chemotherapy
Taxotere	Docetaxel	Chemotherapy
Navelbine	Vinorelbine.	Chemotherapy
Tarceva	Erlotinib	EGFR Inhibitor

Many of the checkpoint inhibitors that are approved in cancer areas outside of NSCLC are currently in combination trials for NSCLC with chemotherapy and other complementary therapies. Pembrolizumab, for example, is being used with decitabine, abraxane, and by itself in a number of trials currently underway. Checkpoint inhibitors are particularly effective in combination therapy because the two drugs can act on multiple immune pathways simultaneously, and in the case of cancer vaccines, will activate T-cells that allow CTLA-4 and PD-1/PD-L1 to achieve their maximum therapeutic potential.

With the promising data from the Phase II trial, we believe Heat Biologics can gather substantial attention from checkpoint inhibitors that are seeking to differentiate themselves. Currently, HTBX is conducting the DURGA combination trial which joins HS-110 and nivolumab (Opdivo).

[6] Borghaei H, et al. NEJM 2015;373:1627-39
[7] Nishio M, et al. JCO 2015; 33:15_suppl, 8027-8027

HS-110 Phase I Trial

Eighteen late stage NSCLC patients were enrolled in an 18 week Phase I trial. Inclusion criteria required that patients be in NSCLC stage IIIB or IV, or have recurrent disease, with stable brain metastasis if present. Patients must have received and failed a minimum of two other lines of therapy and be at least 18 years of age with life expectancy in excess of three months. Additional constraints were present for lab test results, with a focus on liver data. Exclusion criteria include cardiac disease, pregnancy, HIV, uncontrolled metastases and a variety of other cancer treatments or disease.

Allogenic NSCLC tumor cells were used as the source of tumor antigens and developed into a vaccine. The vaccine was administered intradermally in three 6-week courses over an 18 week period. Blood samples were collected before the initial administration. There was one grade II episode related to muscle weakness in a lower limb. We provide a summary of the safety data below.

Exhibit XIII – HS-110 Phase I Adverse Events[8]

Category	AE Short Name	Patients		Episodes	Worst
		N	%		Grade
DERMATOLOGY/SKIN	Induration	18	100%	102	1
DERMATOLOGY/SKIN	Rash	16	89%	124	1
DERMATOLOGY/SKIN	Pruritus	5	28%	11	1
DERMATOLOGY/SKIN	Dermatology/Skin - Other (Specify)	3	17%	11	1
DERMATOLOGY/SKIN	Hypopigmentation	3	17%	7	1
DERMATOLOGY/SKIN	Bruising	2	11%	3	1
DERMATOLOGY/SKIN	Injection site reaction	2	11%	7	1
DERMATOLOGY/SKIN	Hyperpigmentation	1	6%	1	1
PAIN	Pain - Other	2	11%	17	1
NEUROLOGY	Dizziness	1	6%	1	1
HEMORRHAGE/BLEEDING	Hematoma	1	6%	1	1
MUSCULOSKELETAL/SOFT TISSUE	Muscle weakness lower limb	1	6%	1	2
Total				286	

Immune response endpoints were documented by measuring antigen-specific CD8+ cytotoxic T-cells in vaccinated patients. ELISPOT analysis, which is a widely used assay to measure cellular immune responses was employed to detect IFN-γ (which is secreted by cytotoxic T-cells) to determine if there was an immune response. A patient was catagorized as a responder if they had more than a 200% increase from baseline levels.

There were 15 immune responding patients at baseline and a greater than twofold increase in IFN-γ secreting CD8+ cells was observed in 11 of these responders. Four patients had a minimal response after the vaccination, indicating that their immune system was unable to generate an allogenic response. Immune responding patients had estimated median survival of 16.5 months while non-immune responding patients averaged 4.5 months.

While the trial only enrolled 18 patients, a larger group of 36 patients was targeted. However, due to an institutional conflict of interest concern, the trial was closed for reasons unrelated to the study.

HS-110 Phase Ib/II Trial[9]

Heat is conducting a Phase Ib/II trial with HS-110 in combination with nivolumab entitled "A Phase 1b/2 Study of Viagenpumatucel-L (HS-110) in Combination With Multiple Treatment Regimens in Patients With Non-Small Cell Lung Cancer" (The DURGA Trial). The trial was launched in May 2015 and will investigate the benefits of HS-110 used in conjunction with Bristol-Myers' (BMY) PD-1 checkpoint inhibitor Opdivo (nivolumab). The trial was structured with pre-specified thresholds that will enable it to expand it to a full Phase II study. The initial goal of the trial is to enroll 18 patients and provide for cohort expansion of up to 30 per arm[10] for a total of 60 patients. For Phase Ib, the trial's primary endpoint is safety and the secondary endpoint is objective response rate (ORR). For the Phase II segment of the study, the primary endpoint is ORR. Secondary outcome measures include safety of

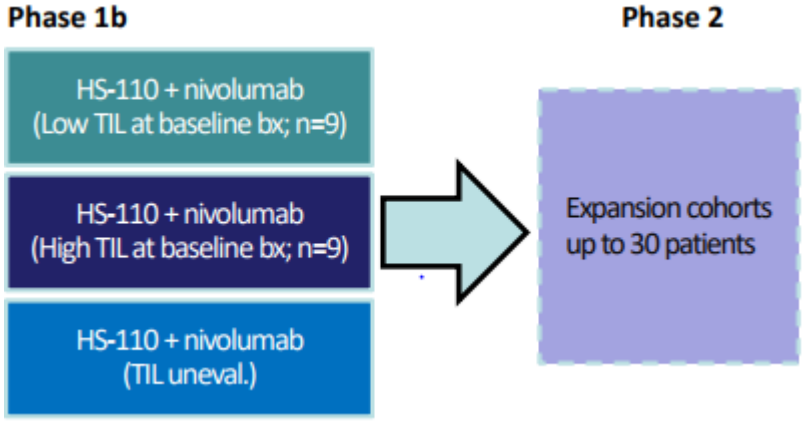
[8] L. E. Raez et al. / Advances in Lung Cancer 2 (2013) 9-18, p. 14.
[9] Morgensztern, Daniel; et al. Viagenpumatucel-L (HS-110) Bolsters Response to Nivolumab Therapy in Advanced Lung Adenocarcinoma: Preliminary Data From The DURGA Trial. December 2016, IASLC 17th World Conference on Lung Cancer. Link here.
[10] The two cohorts will consist of low TIL and high TIL patients

each combination regimen, characterization of the peripheral blood immunologic response on CD8+ cells following vaccination, and progression free survival (PFS) for up to three years following the trial.

Inclusion criteria for the trial require NSCLC patients with prior line of therapy for incurable or metastatic NSCLC. Life expectancy must be greater than 18 weeks, patient must be able to move about with ECOG performance status of 1 or 2, CNS metastases must be stable and lab results must conform with outlined parameters among other minor conditions. Exclusion criteria requires previous cancer treatment greater than three weeks before start.

In the first arm of the Phase Ib trial, patients were assigned to a low tumor infiltrating lymphocyte (TIL) group or a high TIL group with up to 9 patients in each arm. Patients that were not assigned to these arms due to availability of TIL data are assigned to the rollover arm with no limit to enrollment. All patients were administered weekly injections of $1x10^7$ HS-110 cells and nivolumab for 18 weeks or until disease progression or toxicity. 15 patients were ultimately enrolled in the Ib.

Exhibit XIV – HS-110 Phase Ib/II Trial Design



Safety and efficacy endpoints for the Phase Ib portion of the trial were provided mid-March 2017, after which the Phase II began enrollment. The Data Monitoring Committee (DMC) confirmed that safety endpoints were met and that HS-110 did not result in any additional toxicities compared to nivolumab alone. Of the 15 patients enrolled and receiving the combination therapy, one-third showed a greater that 20% reduction in tumor volume, supporting the transition to Phase II. The initial clinical trial saw evidence of an association between higher levels of TILs and a durable benefit, supporing additional study in subsequent trials. Six of the eight patients that presented increased levels of TILs survived beyond the one-year follow-up. In conjunction with this announcement, Heat elected to proceed with Phase II.

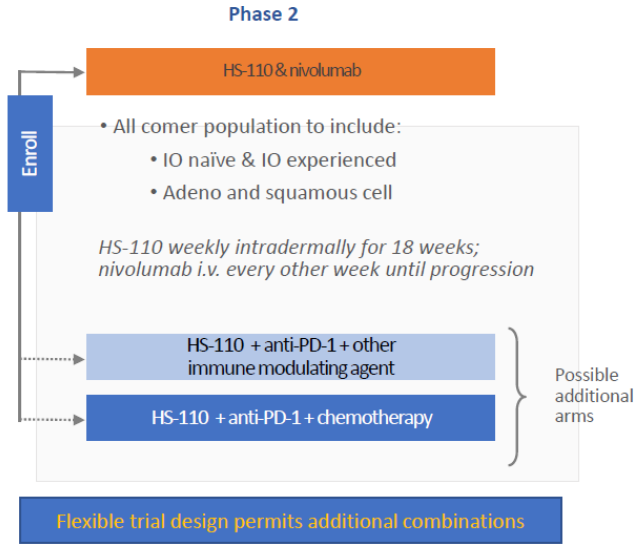
On March 21st, 2017 Heat provided an interim analysis for its Phase II study of HS-110 in combination with nivolumab for NSCLC. As of the announcement date, 15 patients had been treated and 12 of them were evaluable[11] for ELISPOT analysis. Analysis of this 12-person dataset shows a strong correlation between T-cell activation, tumor shrinkage and overall survival. Preliminary key findings from this limited group that was administered HS-110 are:

- The five patients that exhibited tumor shrinkage also had an immune response
- Tumor shrinkage was not seen in patients that did not show an immune response
- There was correlation between immune responses and clinical responses, both of which were sustained
- Five patients were enrolled in the low-TIL cohort, and three of these five patients have shown significant tumor reduction.[12]

[11] Patients were evaluable if a peripheral blood sample was collected and the collection amount was sufficient for evaluation. A minimum of a pre-treatment and on-treatment sample were required. In most cases, if a patient had clinical progression prior to seven weeks on-treatment, ELISPOT was not evaluable.
[12] This compares to a 10% response rate for nivolumab alone. Teng et al, Cancer Research 75(11) June 1, 2015

Exhibit XV – Phase II Trial Design

Objective	• Evaluate objective response rate of HS-110 and anti-PD-1 immune checkpoint inhibitor and other agents
Patient Population	• NSCLC • Adenocarcinoma and squamous cell carcinoma • 2nd line therapy or greater
Endpoints	• Safety and tolerability, immune response, objective response rate, duration of response, overall survival and progression-free survival
Enrollment	• Up to 25 U.S. sites • Up to 120 patients TBD by iDMC • Partnership with Yale Cancer Center on TIL analysis



Of the 15 patients that were administered the HS-110 and nivolumab combination, a third of them exhibited 20% or greater tumor reduction. Eight patients had high levels of TILs demonstrating a more durable benefit with 75% of this subgroup alive at the one year follow-up. While it is too early to hypothesize the survival rate confered by HS-110, preliminary data show a 1-year overall survival rate of 50% for the responders and 25% for the non-responders. Immune responders experienced a better median overall survival at 12.7 months compared to non-immune responders, who saw a median overall survival of 7.1 months. The safety profile was positive with adverse events similar to nivolumab alone.

On February 28, 2018, Heat provided another interim update on its Phase II trial. The combination trial with HS-110 and nivolumab for patients with advanced NSCLC provided favorable results for the 35 patients in the intent to treat population. 17% of the group achieved a partial response and 40% achieved disease control. The evaluable patients in the intent to treat population exhibited overall response rates of 26% and disease control rates of 67%. The drug combination was well tolerated with no additional toxicities compared to nivolumab alone. The results so far have been helpful in gathering data to design a pivotal trial and identifying the best NSCLC population to treat.

In summary, interim data showed a durable and long lasting overall response, despite not yet achieving sufficient duration to determine median overall survival. HS-110 provided evidence of durable responses in difficult to treat low-TIL patients and also in low PD-L1 patients, who generally do not respond well to checkpoint inhibitors. A data readout is expected in 2Q:19, followed by and end of Phase II meeting with the FDA.

Phase III Trials

Heat must complete a Phase III trial before NDA submission. The design of the Phase II trial was adaptive, open label and not randomized or placebo controlled. While this has helped identify optimal dosing strategies and patient profiles that may see increased benefit from the treatment, the design is not sufficient to qualify for FDA expedited action and a Phase III will be required for approval. Based on discussions with management, we anticipate that the Phase III trial may need to enroll from 200 to 300 subjects and employ overall survival, objective response or progression free survival as a primary endpoint. The expected survival for the NSCLC group is from 12 to 18 months, which suggests a three year length assuming a timely enrollment pace. Our assessment of Heat's progress and company guidance suggest an end of Phase II meeting taking place 2H:19 and the Phase III beginning shortly after. Assuming one year to enroll subjects, the trial may be able to close data collection by late 2022 and provide topline analysis shortly after.

Excluding the selected primary measure, secondary endpoints may include progression free survival, overall survival, objective response rate, duration of response and could also include quality of life, health economic analysis and potentially other relevant measures. While it has not been used before, an exploratory endpoint may incorporate ELISPOT analysis which will measure immune response based on its potential for predictive ability.

Other Development Programs

In addition to HS-110, Heat/Pelican has three other compounds in preclinical studies. This includes HS-130, which is HS-110 combined with OX-40 co-stimulator and a checkpoint inhibitor and PTX-35 which is expected to submit an IND by 1Q:19 and start a Phase I trial shortly after.

Exhibit XVI – Heat Biologics Pipeline[13]

Combination Therapies	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Approved	Comments
HS-110 (viagenpumatucel-L)	NSCLC						ImPACT® activation technology in combination with nivolumab and other checkpoint inhibitors TBA
HS-130	NSCLC						ComPACT™ activation technology in combination with checkpoint inhibitors TBA
Co-stimulators							
PTX-35	TBA						Humanized monoclonal antibody, functional agonist of human TNFRSF25 ($15.2M CPRIT grant)
PTX-15	TBA						TL1A-Ig fusion protein, functional agonist of human TNFRSF25

Safety & Adverse Events

A completed Phase I and a Phase II study have generated safety data and another Phase II study is currently being conducted. In the Phase I trial, 18 patients were enrolled and adverse events were grade I with one exception largely relating to skin reactions, pain, dizziness and bleeding. The one grade II was related to muscle weakness in the lower limbs. No grade III or higher reactions were observed.

In a one-year trial which enrolled 8 patients, using HS-110 along with nivolumab (Opdivo), side effects were similar in the combination as they were for nivolumab alone. In this trial, two of the eight enrollees experienced cough, nausea, rash and sinus congestion. In the trial population, each of the following was observed: Anemia, atrial fibrillation, constipation, decreased appetite, diarrhea, dizziness, epistaxis, herpes zoster, hyperkalemia, hypokalemia, hyponatremia, pulmonary embolism, rash, thrombocytopenia and vomiting. The only additional adverse reaction for HS-110 in combination therapy as compared to nivolumab alone is injection site reaction that generally resolves after a week and is easily treated with a topical steroid.

Chemistry, Manufacturing and Control (CMC)

Heat Biologics works with several partners to manufacture and test product. The company's manufacturing partner is Lonza Walkersville, which has manufactured supply of HS-110 for Phase II studies and may continue this role for Phase III. Lonza is a global supplier to the life science industry and is headquartered in Switzerland. Other partners include Shattuck Labs, which is focused on immunotherapy, the Yale Cancer Center which is performing biopsy and TIL analysis and Adaptive Biotechnologies, for analysis of biomarkers.

In September 2017, Heat entered into a manufacturing agreement with KBI Biopharma to develop and manufacture the PTX-35 antibody and PTX-15 fusion protein for Pelican. The manufacturer was founded in 1996 and operates seven facilities in the US and in Europe. Their competencies include cell line development, process, analytical and formulation development, clinical and commercial manufacturing and testing services. Heat sees the relationship as providing advantages in speed, productivity, stability and flexibility over other options for cell line development.

Heat has a process in place which ensures that there are no outstanding warning letters, FDA Form 483s, and that good manufacturing practices (GMP) are followed. Zacks continuously highlights the importance of good practices at partners who perform manufacturing, testing, packaging, fill and finish and other services. This emphasis is justified given the risk of regulatory agency action highlighting partner oversights and focus on partner compliance in spite of a phamaceutical product that is safe and effective.

[13] Source: Heat Biologics Corporate Presentation

Pelican Therapeutics

On March 8, 2017 Heat acquired an 80% interest in Pelican Therapeutics. The company is led by CEO Rahul Jasuja, PhD, an immunologist who previously functioned in a variety of corporate and finance roles. Pelican is focused on the development of monoclonal antibody and fusion protein-based therapies that activate the immune system. Heat paid cash consideration of $500,000 and 1,331,082 shares, which based on the closing price of Heat Biologics on that day valued 100% of Pelican at $2.02 million. As part of the acquisition agreement, Heat has agreed to a number of clinical and commercialization milestones ranging from $2.0 million for first dosing of a patient in a Phase I oncology trial to $7.5 million for ultimate approval in an oncology indication. Heat will also pay a royalty to Pelican following commercialization. Pelican's lead candidate, PTX-35, is a humanized, affinity matured monoclonal antibody that is a functional agonist of human TNFRSF25. The compound can selectively stimulate memory CD8+ cytotixic T-cells.

Based on the company's progress with PTX-35, it was granted $15.2 million from the Cancer Prevention and Research Institute of Texas (CPRIT). Pelican must raise half of this amount in matching funds, equivalent to $7.6 million. The grant covers a three year period from June 1, 2016 to May 31, 2019 to run a Phase I trial for PTX-35 focused on several types of cancers which may include lung, lymphoma, prostate, pancreatic and ovarian. Funds are expected to support IND-enabling studies and enroll 70 patients in a Phase I trial. If the grant-related product eventutally generates revenues, Pelican will pay tiered royalties to CPRIT in the low to mid single digit percent range. After certain undisclosed amounts have been repaid, the royalty rate drops to less than one percent.

In June and October 2017, Pelican received $1.8 and $6.5 million respectively from the CPRIT grant. Pelican is headquartered in San Antonio, Texas and the requirment for accepting the grant calls for all grant-funded research to take place in Texas. We expect the next cash flow and remaining balance from CPRIT to take place in fall 2018. In addition to CPRIT, Pelican also benefitted from an agreement with the City of San Antonio which granted funds to buy $200,000 in laboratory equipment in return for employment obligations over a period of seven years.

Intellectual Property

Heat has been granted over 50 patents worldwide and twenty patents pending as of year-end 2017 for the ImPACT and ComPACT technologies. The company has acquired patents related to therapeutic compositions and methods related to vaccine platform and preclinical development programs. HS-110 is a biologic and is provided 12 years of product exclusivity in the United States, ten years in Europe and eight in Japan following approval by the respective regulatory agencies. Given the difficulties that exist in developing biosimilars, HS-110 could potentially extend its unique market status beyond the end of current protections.

Corporate Milestones

Heat is currently conducting Phase II trials and is seeking a partner to continue development of HS-110. The trial is adaptive, and company guidance calls for a final readout by 2Q:19. Below we list key milestones on the horizon for Heat Biologics. Over the next two years we anticipate the following events.

- Receive $6.9 million in CPRIT grant funds – 3Q:18
- HS-110 (NSCLC) interim data readout - 4Q:18
- ComPACT IND filing – 4Q:18
- ComPACT first patient enrollment – 4Q:18
- IND for PTX-35 – 1Q:19
- Receipt of $6.9 MM in CPRIT grant funds (PTX-35) – 1Q:19
- Enroll first patient in PTX-35 Phase I trial – 1Q:19
- Complete Phase II NSCLC enrollment – 2Q:19
- Interim ComPACT data readout – 2Q:19
- HS-110 Phase II final readout – 2Q:19
- HS-110 End of Phase II Meeting – Mid 2019
- HS-110 NSCLC Phase III ready – 3Q:19
- Interim PTX-35 data readout – 3Q:19
- Discussion with potential partners – 2018 / 2019
- Develop Phase III / commercial manufacturing capacity for HS-110 – 2018 / 2019

RISKS

All investments contain an element of risk which reflects the uncertainty of the business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

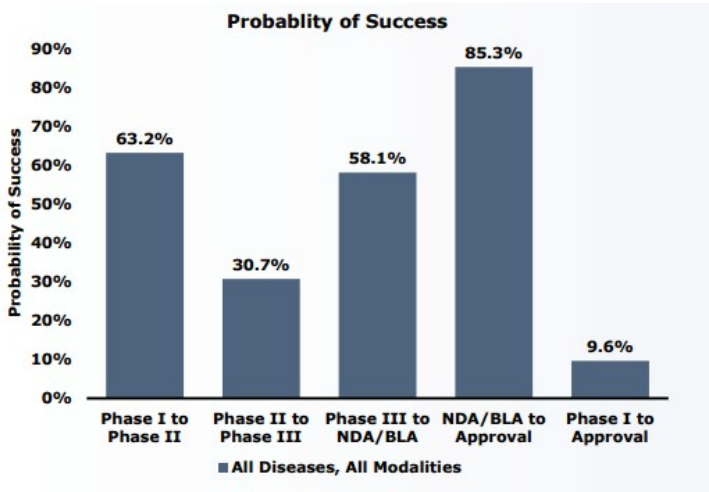
The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products.

For smaller early-stage companies, investing in drug development is an extended process. The timeframe for conducting pre-clinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market conditions. And with, on average, only one in one thousand compounds eventually making it to the market, the risks are substantial.

Even if a company has a strong, experienced team that is developing a therapy with a high likelihood of success and a large addressable market, securing funding may pose a substantial risk. Access to financing comes and goes in cycles. During periods of improving confidence, capital may be easy to access; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. If capital is needed to sustain operations and it is not readily available, the company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route to progress or force a company to accept onerous terms.

All drugs must navigate the regulatory approval process in the US, EU and other countries before commercialization in those regions. This effort is a material uncertainty which may take years depending upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Isolating companies that have a long history of research success in drug development, with opinion leaders and experts in the field are important fundamentals that can help mitigate this risk. Companies that have had previous success with the FDA or other regulatory agencies also are more attractive than those who may be new to the process. Some accelerated pathways to approval have been put forth such as the Orphan Drug Act, however, changes in sentiment or perceived safety for pharmaceuticals drugs could change the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place.

Exhibit XVII – Success of Phased Trials and Regulatory Approval[14]



[14]Clinical Development Success Rates 2006-2015. David Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, Michael Hay.

Currently, Heat is seeking a partner to help develop its lead compound, HS-110, and may depend on financing from this source to advance towards approval. The company plans to conduct this registrational trial after identifying new development partners and consulting with the FDA, both of which may raise additional requirements before moving forward. HS-110 is currently in Phase II trials which have a historical eventual approval rate for all compounds of about 15% and movement on to Phase III trials of 31% as per the preceding graphic.

In recent years, contract research organizations (CROs) have taken on a larger role in the development of drug candidates as the complexity and cost of trials has increased. Finding appropriate populations to participate in clinical trials has become increasingly difficult due to the shift to personalized medicine and orphan indications that address a small population. This shift has increased the dependence on these specialized CROs for project management and clinical monitoring services which add additional risks and dependence on third parties.

In addition to CROs for clinical trials, Heat relies on third parties for manufacturing drug substance, laboratory work and analytical testing services. Risks of poor manufacturing processes, quality control issues and product delays may postpone ultimate production of a drug if partners are out of compliance with regulatory agency requirements. Heat Biologics has developed relationships with its partners and has implemented a process to ensure good practices and compliance. Despite these efforts, the partner may lack the desire or skill to successfully maintain the required good practices and may have other competing products under its control that receive greater attention and focus. Heat and Pelican also have relationships with Lonza Walkersville and KBI Biopharma for manufacturing services and Shattuck Labs, Yale Cancer Center and Adaptive Biotechnologies for laboratory services. Each of these relationships represents a risk that requires careful monitoring from the company in order to ensure regulatory compliance and uninterrupted services.

Drug price inflation has gained increased attention over the last several years and has contributed materially to the increase in health care costs over the last decades. As new therapies have been approved, drug prices have set new records and increased at a substantial rate. For example, in 1996, new cancer drugs cost roughly $54,000 for each additional year of life they provided. However, by 2013, this amount increased to over $200,000. The inflation rate for established drugs has also been very high. In a Forbes article, Novartis' leukemia drug Gleevec was highlighted. This drug cost $24,000 in 2001 when it was first approved; and 14 years later, in 2015, had risen to a cost of $90,000. This represents a 10% compound annual growth rate over that period. Other price moves such as the 5,000% price hike for Turing Pharmaceutical’s Daraprim and Valeant Pharmaceuticals 500% and 200% price increase for Isuprel and Nitropress combined with similar moves by other companies may create a situation where further increases are unsustainable. We also cite the broad response to Mylan’s (NASDAQ: MYL) EpiPen price increases which have pressured the company to offer lower priced alternatives and brought a number of competitors into the market.

We highlight several risks that come from these pricing increases. Health care may become unaffordable for a broad segment of the population, reducing the market size to a level below current expectations. Pharmacy benefit managers and other third party payers may continue to remove drugs from their formularies due to price concerns and sharp price increases will attract the attention of elected officials and regulators who may create legislation and implement regulations that limit drug profitability. Additionally, the government may impose additional non-price related regulation and disclosure requirements that can increase costs for the industry.

While we have discussed a broad variety of risks above, we believe that our forecast parameters, discount rates, success probabilities and valuation metrics address these eventualities and our target price reflects an assumption of these risks faced by all biotechnology companies.

COMPETITORS AND COMPETING THERAPIES

There are many participants in cancer immunology with a variety of approaches from all over the globe including checkpoint inhibitors, CAR-T, oncolytic viruses, antibody drug conjugates and cancer vaccines to name a few. Below, we highlight several of the key companies that are developing cancer immunotherapies in adjacent spaces to Heat. This list is not exhaustive and only represents a cross section of the immunotherapy companies participating in the space.

Exhibit XVIII – Peers and Competitors[15]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
NVS	Novartis AG	$77.29	$198,169	$208,350	Diversified Pharmaceuticals
MRK	Merck & Co	$62.30	$167,606	$183,660	Diversified Pharmaceuticals
GILD	Gilead Sciences	$76.75	$99,790	$104,030	Diversified Pharmaceuticals
BMY	Bristol-Myers	$56.18	$91,828	$93,380	Diversified Pharmaceuticals
AZN	AstraZeneca	$35.60	$89,510	$105,110	Diversified Pharmaceuticals
SGEN	Seattle Genetics	$69.29	$10,960	$10,480	Cancer IO
BLUE	Bluebird Bio	$177.50	$8,900	$7,550	Cancer IO
NKTR	Nektar Therapeutics	$47.12	$8,080	$8,110	Cancer IO - IL-2 Activation
ADRO	Aduro Biotech	$7.20	$567	$283	Cancer IO
AGEN	Agenus Inc	$2.25	$234	$206	Cancer IO
IMV	Immunovaccine Inc	$5.05	$223	$201	Cancer IO
NLNK	NewLink Genetics	$4.81	$179	$38	Cancer IO
ADXS	Advaxis	$1.44	$76	$25	Cancer IO
CLDX	Celldex Therapeutics	$0.52	$74	($49)	Cancer IO
IMUC	ImmunoCellular Therapeutics	$0.25	$10	$6	Cancer IO
BAVA	Barvarian Nordic A/S	DKK 194	DKK 6,260	DKK 3,977	Cancer IO
OXB.l	Oxford Biomedica plc.	£9.22	£606	£629	Cancer IO
TNG.PA	Transgene	€ 3.11	€ 193	$137	Cancer IO, Oncolytic Viruses
pvt	Checkmate Pharma				Cancer IO - TLR9 agonist
HBTX	Heat Biologics	$0.53	$19.1	$10.71	Cancer IO

NVS – Received September 2017 approval for CAR-T therapy Kymriah for B-cell acute lymphoblastic leukemia.

MRK – Manufacturer of pembrolizumab, a widely used checkpoint inhibitor.

GILD – Acquired Kite Pharma and CAR-T therapy Yescarta which was approved in October 2017 for relapsed or refractory large B-cell lymphoma.

BMY – Has developed several drugs that may be used in combination with vaccine therapy such as nivolumab (which is being used in combination trials with HS-110), paclitaxel and ipilimumab.

AZN – A dominant player in the oncology space. Recently suffered setback with Imfinzi for NSCLC which did not meet its primary endpoints in a Phase 3 trial. Favorable results for PARP Lynparza in ovarian cancer trial with MRK.

SGEN – Developing portfolio of antibody drug conjugates (ADCs) including brentuximab vedotin, enfortumab vedotin, ladiratuzumab vedotin and tisotumab vedotin.

BLUE – Developing gene therapies for cancer as well as CAR-T and T-cell receptor programs. In partnership with CELG to develop bb2121 and bb21217 for multiple myeloma which are Phase II/III and I/II assets.

NKTR – NKTR-214 is CD122 agonist in multiple trials with checkpoints and other IO compounds for multiple tumor types.

ADRO – Pursuing STING and B-cell targets and employing listeria bacteria in a variety of cancer indications. The lead candidates are ADU-S100 and BION-1301.

[15] Price and market capitalization data is as of July 10, 2018.

AGEN – IO company developing a broad pipeline of checkpoint inhibitors and vaccines for cancer. Most advanced cancer candidates are a PD-1 and CTLA-4 antagonist and Prophage, a Phase II vaccine for glioblastoma.

IMV – Developing its DepoVax platform, including lead candidate DPX-Survivac which is a T-cell activating immunotherapy. DPX-Survivac in multiple Phase I and II trials for ovarian, DLBCL and HPV-related cancers.

NLNK – Developing two IO agents in a variety of indications with IDO inhibitor Indoximod most advanced. Lead agent in multiple Phase I and II trials for pancreatic, prostate, AML and brain cancers.

ADXS - Developing axalimogene filosisbac in multiple checkpoint inhibitor combination trials for cervical and head & neck cancer in conjunction with AZN and BMY. Also Phase II asset, ADXS-PSA for prostate cancer with Merck's pembrolizumab. Additional IO preclinical assets in development.

CLDX – Developing therapeutic antibodies, antibody drug conjugates, immune system modulators and other protein-based therapeutics in several cancers including breast, melanoma, solid tumors and renal cell carcinoma.

IMUC – Targets cancer stem cells with lead candidate ICT-107. Program suspended pending additional financial resources.

BAVA – Broad pipeline of candidates in cancer and viruses. Oncology portfolio is built on its CV301 IO candidate for multiple cancers. Previous Phase III candidate Prostvac was discontinued on poor data.

OXB – Focused on gene and cell therapy with multiple cancer indications in both preclinical and human trials.

TNG – French biotechnology company employing a portfolio of therapeutic vaccines and oncolytic viruses. Most advanced candidate is Pexa-Vec, which is participating in Phase III combination trial for hepatocellular carcinoma.

Checkmate Pharmaceuticals – Developing CMP-001, a TLR9 agonist. The compound is in a Phase Ib study in combination with pembrolizumab targeting melanoma.

MANAGEMENT PROFILES

Jeffrey Wolf, Chairman and Chief Executive Officer

Mr. Wolf founded Heat Biologics in August 2008. Prior roles include managing director at Seed-One Ventures, a venture firm focused on launching and growing early stage healthcare companies, where he served from June 1997 to March 2011. Since founding Seed-One, Mr. Wolf has founded and run several biomedical companies including Avigen, a gene therapy company where he was a co-founder and director; TyRx Pharma, a company focused on the development of bio-compatible polymers where he was a co-founder and Chairman; EluSys Therapeutics, a company focused on the development of a novel technology to remove blood-borne pathogens where he was a co-founder, Chairman and CEO; and GenerationOne, a company focused on mobile-based collaborative care, where he was the founder, Chairman and CEO. Mr. Wolf received his MBA from Stanford Business School, his JD from New York University School of Law and his BA from the University of Chicago, where he graduated with honors in Economics. Heat's CEO serves as a director of several Seed-One portfolio companies and serves as a director of Synthetic Biologics, Inc., a biotechnology company focused on the development of novel anti-infective biologic and drug candidates targeting specific pathogens that cause serious infections and other diseases.

Jeff Hutchins, Ph.D., Chief Scientific and Operating Officer

Dr. Hutchins joined Heat on January 1, 2017 and oversees the company's research efforts, bringing over 24 years of research and clinical development experience from large pharmaceutical and biotechnology companies. Most recently and since 2012, Dr. Hutchins served as VP of Preclinical Research for Peregrine Pharmaceuticals, Inc., a biopharmaceutical company developing therapeutics to fight cancer and infectious diseases. Dr. Hutchins was responsible for building out the research program for Peregrine's lead product candidate, bavituximab, a chimeric monoclonal antibody designed to target phosphatidylserine. Prior to joining Peregrine in 2012, from 2001 until 2012, Dr. Hutchins served as VP, Preclinical Development at Inhibitex Inc, which was acquired by Bristol-Myers Squibb. From 1991 to 2000, Dr. Hutchins held several senior scientist positions in Discovery Research at Burroughs Wellcome and Glaxo Wellcome, with a visiting professor appointment at Rush Medical College. Dr. Hutchins earned a BS in Biology from Oral Roberts University, a PhD in Biomedical Sciences from the University of Texas, Health Science Center at the MD Anderson Cancer Center and conducted postdoctoral training in the University of Southern California's Department of Microbiology at the Norris Cancer Center. Dr. Hutchins' publications and patents span the fields of oncology, infectious disease, osteoarthritis and immunology.

Ann Rosar, MBA, Vice President of Finance, Controller and Secretary

Ms. Rosar joined Heat Biologics as Controller January 2015 and has over twenty years of experience in finance with publicly held companies and more than fifteen years of experience regarding regulatory reporting requirements. Prior to serving as Heat's Controller, Ms. Rosar served as Manager of Financial Reporting and Accounting for LipoScience, Inc. (acquired by LabCorp), a provider of specialized cardiovascular diagnostic tests, from 2013 to 2015. From 2007 until 2013 she served in various roles at DARA Biosciences, Inc. (now Midatech Pharma US), an oncology supportive care pharmaceutical company, including the VP of Finance, Chief Accounting Officer and Controller. Ms. Rosar was the Manager of Financial Reporting and Accounting with Cicero, Inc. (formerly Level 8 Systems), a provider of business integration software, from June 2000 until November 2007, where she was responsible for SEC reporting, audits and budget analysis. Prior to that position, she served as Senior Financial Analyst-Business Operations for Nextel Communications. Ms. Rosar received a MBA in Finance from the University of Houston and received her undergraduate degrees from North Carolina State University.

George Peoples, M.D., FACS, Chief Medical Advisor

U.S. Army, COL (ret) George E. Peoples, MD, FACS, serves as CMO for both Heat Biologics and its subsidiary, Pelican Therapeutics. Dr. Peoples is currently professor of surgery at Uniformed Services University of the Health Sciences, as well as adjunct professor of surgical oncology at MD Anderson Cancer Center (MDACC). He is also the founder and director of Cancer Insight, LLC, a clinical research and development organization dedicated to the discovering, development and testing for emerging biotechnologies specializing in cancer immunotherapy. Dr. Peoples recently retired from 30 years of active duty as a surgeon and as a research scientist in the Army. He is the past chair of the cancer program at the San Antonio Military Medical Center, and the past deputy director of the United States Military Cancer Institute. Prior to that, he served as chief of surgical oncology at Walter Reed Amy Medical Center (WRAMC), as well as SAMMC. He is a graduate of the United States Military Academy, West Point and Johns Hopkins School of Medicine. Dr. Peoples completed his surgical training at Harvard's Brigham and Women's Hospital, and during that time, also completed a post-doctoral fellowship at the Laboratory of Biologic Cancer Therapy at Harvard Medical School. He then completed a surgical oncology fellowship at MDACC. Dr. Peoples has written extensively on the immune response to cancer, with over 300 peer-reviewed manuscripts, abstracts and book chapters.

Janice Marie McCourt, RPh, MBA, Executive Vice President, Business Development

Janice Marie McCourt, leads business development and partner alliances. She has 25 years of experience leading pharma and biotech companies globally; working across the R&D-to-commercial continuum in business development, commercial and clinical development. Ms. McCourt has raised over $3 billion in global licensing, acquisition, investment and partnerships. Previously, she led the strategic and tactical diversification of Agenus from a vaccines-focused company directly into the antibody checkpoint modulation space with the acquisition of 4-Antibody, thereby establishing the company as a leader in immuno-oncology. Ms. McCourt has been on executive management teams, leading commercial strategy and business development at Edgemont Pharmaceuticals, Amakem Therapeutics and Praecis Pharmaceuticals (now GSK). She spent five years at Ingenix, the $1.5 billion consulting arm of UnitedHealth Group, leading both commercial and development projects with top-tier pharmaceutical and biotech companies. As the first commercial hire at TAP Pharmaceuticals, she was promoted numerous times in various management commercial roles. She has led many product launches for major brands in immuno-oncology, CNS, immunology, inflammation, women's health, neurology, respiratory, ophthalmology, infectious disease, vaccines and pain therapeutic areas. Ms. McCourt graduated from Massachusetts College of Pharmacy and Allied Health Sciences, where she completed her clinical rotation at Harvard Medical School on the internal medicine, gastroenterology, and cardiac units, and also has an MBA with high honors.

Lori McDermott, RN, BSN, MS, PMP, Vice President, Clinical Development

As VP of clinical development, Lori McDermott oversees the strategic and operational aspects of clinical drug development for Heat Biologics, as well as for the company's subsidiary, Pelican Therapeutics. Ms. McDermott brings more than 18 years of clinical operations and program management experience, spanning across large and small pharmaceutical companies, as well as contract research organizations. Prior to joining Heat Biologics, Ms. McDermott held positions of increasing responsibility at Astra-Zeneca, ICON, Bausch & Lomb, PPD and Peregrine Pharmaceuticals. Ms. McDermott's responsibilities have included the execution of clinical trial programs, from Phase 1 to 4, with a recent focus on immunotherapy development in non-small cell lung cancer. Prior to her work in clinical research, Ms. McDermott practiced as a registered nurse and is currently licensed in Pennsylvania and Florida. Ms. McDermott received an M.S. in clinical research organization and management from Drexel University College of Medicine, and her B.S. in Nursing from Neumann College. She is also certified as a PMP by the Project Management Institute.

Gary Vinson, Vice President, Chemistry and Manufacturing Controls (CMC)

As VP of Chemistry and Manufacturing Controls, Gary Vinson is responsible for all manufacturing and analytical development for Heat Biologics, as well as for the company's subsidiary, Pelican Therapeutics. He has more than 20 years of experience in the pharmaceutical, CRO/CMO and biotechnology industries, in technical, development and quality roles. Prior to joining Heat, he held roles as VP, Pharmaceutical Development at a specialty pharmaceutical company, BioDelivery Sciences, and at Aldagen, a clinical-stage regenerative medicine company developing adult cell therapies. His responsibilities have included leading manufacturing, analytical development and quality organizations, and he has significant experience developing CDMO outsourcing relationships from pre-IND through to registration. Mr. Vinson founded and was Managing Partner of The Perdoceo Group, LLC, a consulting firm providing CMC support to biotechnology and pharmaceutical clients. He began his career with Glaxo, Inc. and worked at Magellan Laboratories, where he was a principal in establishing the pharmaceutics group to provide contract development and manufacturing of clinical trial materials. Mr. Vinson received his BS in Chemistry from North Carolina State University and holds CPGP (Certified GMP Professional) and RAC (Regulatory Affairs Certification) certifications.

Rahul Jasuja, PhD, CEO, Pelican Therapeutics

Dr. Jasuja previously served as Senior Biotechnology Analyst at FBR & Co., as well as Managing Director, Biotechnology Research, at Noble Life Science Partners (NLSP). Prior to NLSP, Dr. Jasuja was VP of Corporate Development at Idera Pharmaceuticals, focused on developing Toll-like receptor based immune-modulators. He has also held progressively senior positions within the biotechnology capital markets at Techvest LLC, Rodman & Renshaw and MDB Capital Group. Dr. Jasuja brings more than 20 years of experience in the biotechnology field, including corporate/business development, technology due-diligence, equity research and academic research. Rahul received his PhD in Immunology from Tufts University School of Medicine in which he explored aspects T-cell activation and the subsequent regulation of adhesion receptors in the immune response. He conducted doctoral and post-doctoral research at Harvard Medical School, in the Department of Hematology & Oncology at Beth Israel Deaconess Medical Center. Dr. Jasuja obtained his BSc in Microbiology & Biochemistry from the University of Bombay and an MS in Microbiology from the University of Montana, Missoula, where he studied the role of bacterial cell wall immune modulators on arachidonic acid metabolism and inflammatory pathways in macrophages.

Financial Results

Heat Biologics distributed a press release announcing first quarter 2018 results on May 15, 2018 in conjunction with their 10-Q SEC filing. The key development in the period was the positive interim results from the Phase II study of HS-110 and nivolumab. The release of favorable data was followed by a capital raise of $20.7 million which is expected to support the completion of enrollment in the Phase II trial, enroll for the ComPACT trial, launch the Phase I study for PTX-35 and report preliminary data for these studies. Heat also added to its scientific advisory board and adopted a stockholder rights plan. Management team members attended several investor and scientific conferences during the period.

Revenue of $750 thousand represents funds recognized in conjunction with the CPRIT grant to develop Pelican's co-stimulator, PTX-25. Total operating expenses were $4.7 million, representing a 40% increase over the prior year. Research and development rose 58% due to greater spending on the HS-110 related to patient enrollment and the PTX 35/15 programs, slightly offset by the wind down of HS-410. General and administrative costs rose 17% to $1.8 million on account of higher personnel costs related to growth in the Texas operations associated with Pelican. On a per share basis, net loss was ($0.75), compared to a loss of ($1.18) in the first quarter 2017. Share count expanded to 4.7 million shares over the prior year due to stock issuance and warrant exercise.

The balance sheet indicates $9 million in cash and equivalents and no debt as of March 31; however, subsequent to the close of the quarter Heat raised $21 million gross in new funding. Cash used in operations for the first quarter of 2018 was ($3.8) million. Capital expenditures were a modest $419 thousand. Together, these cash flows produce a quarterly cash burn of ($4.2) million which is equivalent to approximately ($1.4) million per month.

VALUATION

Heat's lead candidate, HS-110, is a cancer vaccine developed through the use of the company's proprietary ImPACT technology. HS-110 is able to generate an antigen specific immune response to NSCLC by leveraging the heat shock protein gp96. The cells that are used in the agent excrete a protein that both alerts the immune system to a potential threat and also provides specific antigen identification of this threat. While HS-110 has shown efficacy in monotherapy, it is expected to be even more successful when used in combination with other therapies such as checkpoint inhibitors or co-stimulatory monoclonal antibodies. HS-110 has several advantages as an allogenic therapy that can address multiple antigens related to NSCLC cells.

HS-110's lead indication is for non-small cell lung carcinoma, which can pursue a market of over 175,000 persons per year in the United States and almost 1.5 million outside the US. Heat's pipeline is also augmented by several co-stimulators which may enhance the function of ImPACT. Heat held a Type C meeting with the FDA to discuss the registrational requirements for HS-110 in December and also plans to present data generated to date with potential collaborators as it determines the next steps for a confirmatory trial. Our valuation does not attach any value to preclinical assets in the portfolio.

While the company has not provided guidance on timing for the anticipated start for a registrational trial, we anticipate this will occur in 2H:19. We estimate a Phase III trial duration of three years and regulatory review of one year which predicts FDA approval in 2023 for HS-110 in NSCLC. Heat has not defined the NSCLC setting that they will pursue. Therefore, our model assumes a low penetration into the broad NSCLC setting, which can be adjusted as conditions change with minimal impact on net volumes from a higher penetration in a more specific setting. For pivotal work, Heat may take all comers or segment second line therapy or identify a biomarker. Tradeoffs between the approaches are market size, speed of approval and the ability to enrich the patient population sufficiently to focus on those most likely to succeed. In any case, Heat will pursue the indication in NSCLC with a combination therapy of HS-110 and a checkpoint inhibitor.

Based on these assumptions, our estimates forecast a 2023 launch and initial penetration in the US to start in the low-single digits and rise to 8% after four years. We note that HS-110, if successful, will likely be used in conjunction with checkpoint inhibitors and perhaps additional therapies. Penetration outside the US is anticipated to follow a similar trajectory, and HS-110 is forecast to obtain approval and launch in 2024 in Europe and 2025 in the rest of the world.

While it is still too early to estimate the overall survival rate for HS-110, its effectiveness in preclinical work suggests value can be maintained on par with other immunotherapies. Compared to other autologous approaches (such as in CAR-T), HS-110 has a relatively low cost of goods which provides a substantial amount of flexibility for pricing. Based on other approved cancer immunotherapies that are priced in the mid-$100,000 range for a course of treatment, we apply a sharp discount for HS-110 given the early stage of development and the anticipated increased competitive and pricing environment when approval occurs. Based on these parameters, we estimate a realized price of $60,000 per treatment cost in the United States, with appropriate discounts in the EU ($30,000 per course of treatment) and an additional reduction in the rest of the world ($18,000 per course of treatment).

Additional discounts are applied to sales outside the United States which reflect the price differentials among the US, Japan and EU markets. We used a list of seven[16] drugs to determine our ~50% adjustment for pricing in Europe[17] and apply additional discounts to other markets which include less developed economies.

We anticipate that Heat will obtain a partner for Phase III or registrational trials and commercialization of HS-110 worldwide due to the difficulties of building a salesforce in numerous unique and challenging regions. Our model assumes an overall 20% transfer of value (represented as a royalty payment) from the commercializing entity to the developer due to the anticipated partnership beginning prior to registrational trials. While we anticipate the normal licensing structure of upfront payment, royalty and milestones, for simplicity we have assumed all value from the arrangement is represented in the royalty payment.

R&D and administrative expenses are anticipated to be ~$18 million in 2018 and rise to ~$30 million at product launch in 2023. These amounts will grow at normal inflationary rates following an R&D reset in 2024. Taxes, which will be paid after the company works through its NOLs, are anticipated to be 30%, in a mix of US federal and state

[16] Crestor, Lantus, Advair, Solvadi, Humira, Herceptin, Gleevec
[17] https://www.bloomberg.com/graphics/2015-drug-prices/

rates. This includes a 21% rate for federal taxes, a 5% rate for state taxes and an additional 4% to reflect tax increases that reflect reversals to deficit spending or shift of tax burden to states.

Our target price is generated using forecasts over the next 20 years after which we assume a terminal growth rate of 2%. We anticipate that some as yet unidentified alternate therapy will begin to compete with HS-110 over the forecast period due to the substantial amount of research that is being done in this space and the accelerating pace at which research is taking place. Therefore we begin to reduce penetration rates for HS-110 in 2032. Assuming a 2023 approval by the FDA, biologic exclusivity for HS-110 will expire in 2034, however, due to innovation and the difficulties in creating biosimilars, we do not anticipate a material impact from this expiration. We use a discount rate of 15% in our NPV model and apply a 15% probability of FDA approval and ultimate commercialization based on the guidance provided in the Biomedtracker analysis.[18]

Based on the assumptions above and after adjusting for shares, restricted stock and options outstanding, we generate a target price of $5.00.

CONCLUSION

HS-110 has shown early efficacy in activating T-cells to recognize tumor cells, evidence of synergies in conjunction with checkpoint inhibitors and co-stimulators in NSCLC and has a record of safety in 200 patients that have been treated in several trials. Based on the structure of the Phase II, HS-110 will pursue a Phase III registrational trial which we anticipate will provide topline data in 2022. NSCLC is an immense market that may represent as many as 175,000 cases in the US and a multiple of that size beyond its borders. Based on the initial data generated in the Phase II trial, Heat is in a strong negotiating position with the multitude of checkpoint inhibitors that require complementary therapies. With the higher response rate from patients with hot tumors, and HS-110's ability to stimulate T-cells, the drug is in a position to complement an established company's portfolio.

Key reasons to own:

- **Compelling preclinical and clinical data supportive of effective mechanism of action**
- **Differentiated approach that employs multiple proteins for cancer cell identification**
- **Evidence of synergy with checkpoint inhibitors**
- **May address critical need for complementary therapies in NSCLC**
- **Pipeline of additional co-stimulatory assets complementary to HS-110**
- **Favorable drug safety profile with minimal adverse events**
- **Biologic eligible for 12 years of exclusivity in United States**
- **Global rights to intellectual property**
- **Manufacturing process produces high yields at low cost, in contrast to other biologics**

In summary, we believe that if HS-110 is able to continue to generate positive data in combination therapy for NSCLC, the shares are undervalued relative to their potential. While our valution only accounts for sales of HS-110, the company has other candidates in development that could yield value as great as HS-110. Based on our analysis and forecasts, we initiate Heat Biologics with a target price of $5.00.

[18] Clinical Development Success Rates 2006-2015. David W. Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, Michael Hay.

PROJECTED FINANCIALS

Heat Biologics, Inc. - Income Statement

Heat Biologics Inc.	2017 A	Q1 A	Q2 E	Q3 E	Q4 E	2018 E	2019 E	2020 E
Licensing	$1.5	$0.8	$1.2	$1.2	$1.2	$4.4	$4.8	$2.8
YOY Growth								
YOY Growth								
Total Revenues	**$1.5**	**$0.8**	**$1.2**	**$1.2**	**$1.2**	**$4.4**	**$4.8**	**$2.8**
YOY Growth								
Research & Development	$8.3	$2.9	$2.4	$2.4	$2.4	$10.1	$15.0	$16.2
General & Administrative	$6.4	$1.8	$1.9	$1.9	$2.0	$7.5	$8.0	$8.2
Other	$0.2	$0.0	$0.0	$0.0	$0.0	$0.0		
Income from operations	($13.3)	($3.9)	($3.1)	($3.1)	($3.2)	($13.3)	($18.2)	($21.6)
Operating Margin	*-878%*	*-520%*						
Pre-Tax Income	($13.2)	($3.7)	($3.1)	($3.1)	($3.2)	($13.3)	($18.2)	($21.6)
Provision for Income Tax	$0.8	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*-6.1%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	**($12.4)**	**($3.7)**	**($3.1)**	**($3.1)**	**($3.2)**	**($13.3)**	**($18.2)**	**($21.6)**
Non-controlling Interest	($0.6)	($0.2)	($0.2)	($0.2)	($0.2)	($0.8)	($0.8)	($0.8)
Net Income After NCI	**($11.8)**	**($3.5)**	**($2.9)**	**($2.9)**	**($3.0)**	**($12.5)**	**($17.4)**	**($20.8)**
Net Margin	*-816%*	*-496%*						
Reported EPS	**($3.08)**	**($0.75)**	**($0.18)**	**($0.14)**	**($0.14)**	**($0.79)**	**($0.76)**	**($0.74)**
YOY Growth	*-56.9%*	*-36.7%*	*-80.2%*	*-78.5%*	*-83.0%*	*-74%*	*-4%*	
Basic Shares Outstanding	3.85	4.71	16.00	21.00	21.30	15.75	23.00	28.00

Source: Company Filing // Zacks Investment R

© Copyright 2018, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE

Heat Biologics, Inc. – Share Price Chart



DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, John Vandermosten, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.

Zacks SCR has received compensation from the issuer directly or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Heat Biologics, Inc. engaged Zacks Investment Research to provide research and distribution services at an annual rate $20,000. This research report was prepared under the aforementioned engagement.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.

© Copyright 2018, Zacks Investment Research. All Rights Reserved.